Responsiveness to ADHD treatment may be determined by neuroanatomy

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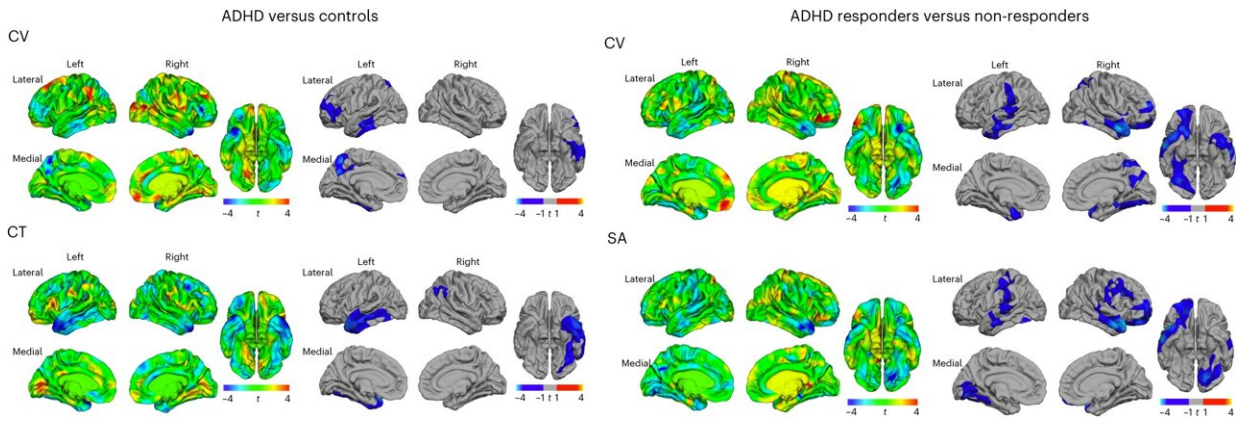

Vertex-wise comparisons between ADHD (N = 60) and controls (N = 23), and between ADHD responders (N = 42) and non-responders (N = 18). Credit: *Nature Mental Health* (2024). DOI: 10.1038/s44220-024-00228-y

New research from the Institute of Psychiatry, Psychology & Neuroscience (IoPPN) at King's College London has found that the effectiveness of ADHD medication may be associated with an individual's neuroanatomy.

The research, published in *Nature Mental Health*, suggests that the development of clinical interventions for ADHD could benefit from identifying how the brain anatomy of treatment-resistant individuals may differ from that of individuals that respond to medication.

Investigators studied individual responses to two-month methylphenidate (MPH) treatment, the prescription medication typically used to treat ADHD, in 60 adults with ADHD. Using MRI, they compared brain anatomy between individuals with ADHD and neurotypical controls, and, among individuals with ADHD, between those that responded and those that did not respond to treatment.

Finally, to better understand their findings, they mapped anatomical group differences onto brain maps of gene expressions.

Researchers found that adults with ADHD who were not responsive to MPH had significant differences in their brain anatomy as compared to both those that responded and controls. These anatomical differences meant that their attention improved less when taking treatment.

Some group differences between individuals with ADHD and controls were associated with differences in the expression of genes related to the transport of noradrenaline, a known target of ADHD medications.

Though MPH is generally effective in improving ADHD symptoms, these findings may help researchers and clinicians understand previous randomized controlled trials which have reported that more than one third of adults do not respond to MPH.

"These findings suggest that those who respond to MPH and those who do not may represent different biological subgroups within the adult ADHD population. This work can help us understand why treatments for ADHD are not universally effective, which will ultimately help to advance the development of more targeted clinical interventions," says Dr. Valeria Parlatini.

The study focused only on male individuals, with ADHD more commonly diagnosed in men and following preliminary evidence of sex

differences in brain anatomy and biological response to stimulants.

"This is one the first studies to investigate differences in neuroanatomy related to treatment response that focused solely on adults with ADHD. Anatomical studies to date comparing responders and non-responders included only children or a mixed sample of children and adults, did not include neurotypical controls for comparison, and have mostly been based on volumetric measures," says Professor Declan Murphy.

Researchers note the results need to be replicated and extended in further independent studies to increase understanding of why certain individuals are resistant to treatment.

This would in turn help advance the development of clinical interventions by identifying treatment resistant individuals in the context of clinical trials of new treatments.

More information: V. Parlatini et al, Cortical alterations associated with lower response to methylphenidate in adults with ADHD, *Nature Mental Health* (2024). DOI: 10.1038/s44220-024-00228-y

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